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EDTN
HPV TEST PLAN

Submitted to the U.S. Environmental Protection Agency

By

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SUMMARY

Akzo Nobel Functional Chemicals LLC has sponsored ethylenediaminetetraacetonitrile (CAS# 5766-67-6), also known as EDTN, in the U.S. EPA High Production Volume (HPV) program. Although there are no experimental data on SIDS endpoints for EDTN, data exists on these endpoints for propylenediaminetetraacetonitrile (CAS# 110057-45-9), also known as PDTN and an analog of EDTN. This document will identify EDTN as a closed system intermediate making it exempt in the HPV program from testing of some SIDS endpoints and justify the use of PDTN data.

Robust summaries of studies on PDTN and EDTN are included in this submission. Data on EDTN from the EPIWIN computer model were used in the absence of experimental values on PDTN for boiling point, photodegradation and fugacity. EDTN data were also used to compare with PDTN experimental values for other environmental chemistry endpoints to show similarities between the two chemicals and support the use of PDTN data for mammalian toxicity and ecotoxicity endpoints. The table below summarizes the endpoints of interest in the HPV program, the available data, and indicates proposed testing.

Endpoint	Data Available & Sufficient	Testing Proposed
Physical/Chemical Characteristics	Yes	No
Photodegradation	Yes	No
Hydrolysis	Yes	No
Biodegradation	Yes	No
Transport	Yes	No
Acute Fish Toxicity	Yes	No
Acute Daphnia Toxicity	Yes	No
Acute Alga Inhibition	Yes	No
Acute Toxicity	Yes	No
Genetic Toxicity	Yes	No
Repeated Dose	Yes	No
Reproductive Toxicity	N/Ap	N/Ap
Developmental Toxicity	No	Yes

N/Ap – Not applicable

1.0 INTRODUCTION

Akzo Nobel Functional Chemicals LLC has sponsored EDTN (CAS# 5766-67-6) in the U.S. HPV program to assess its health and environmental hazards, including selected physical/chemical characteristics. In the absence of data on EDTN, data on the structurally similar chemical, PDTN (CAS# 110057-45-9), will be used.

This document includes identification of EDTN as a closed system intermediate and justification for the use of PDTN data. The justification for the latter is based on similarities in chemical structure, physical/chemical properties and metabolism between EDTN and PDTN. In addition, an evaluation of the available toxicity data and proposed test plan are included.

It is proposed that a developmental toxicity study be conducted on EDTN.

2.0 EDTN: A CLOSED SYSTEM INTERMEDIATE

EDTN, which is an intermediate in the production of EDTA, is synthesized by a reaction of 1,2 ethylenediamine, formaldehyde and cyanide. In this process, a ratio of four moles of formaldehyde and cyanide to one mole of 1,2 ethylenediamine are used.

EDTN is manufactured at an Akzo Nobel facility in the U.S. and transported for use as an intermediate to three sites, two of which are outside the U.S. EDTN is transported in reusable large bags (woven polypropylene, UV stabilized, dust free seams) by trucks within the U.S. with the bags properly labeled with product safety information. At the EDTA production sites, the bags containing EDTN are stored in a warehouse. When needed for synthesis of EDTA, EDTN is transported by forklift from the warehouse to the manufacturing plant where the large bags are emptied into a reactor. In the reactor, a slurry is made of EDTN and water and then EDTN completely reacts in an alkaline environment to produce EDTA.

EDTN is a wet cake so the risk of worker exposure is low. However, plant operators wear masks and gloves to further reduce any chance of exposure. The bags are returned to the U.S. manufacturing facility to be used again. When the bags can no longer be used, they are sent to a recycling facility. The waste from the reactor following production of EDTN in the U.S. is sent to an EPA approved deep well at the manufacturing site. The waste from the reactor contains approximately 0.03% of EDTN.

Although measurements for residual levels of EDTN in EDTA have not been done, it is extremely unlikely that EDTN will be found in EDTA. EDTN is hydrolyzed in caustic during the production of EDTA with all nitrile groups of EDTN reacting during the process. This is followed by addition of an inorganic acid to EDTA at high temperatures resulting in a final product pH of less than 2.

3.0 PDTN: AN ANALOG

The structures of EDTN and PDTN are seen below.

EDTN $(CH_2\text{-}CN)_2$ - N - $(CH_2)_2$ - N - $(CH_2\text{-}CN)_2$
PDTN $(CH_2\text{-}CN)_2$ - N - $(CH_2)_3$ - N - $(CH_2\text{-}CN)_2$

The structures show that the only difference is that PDTN has one more carbon atom between the two nitrogens. Both chemicals have four identical acetonitrile groups which determine the function and reactivity of EDTN and PDTN. Due to the similarity, it is not unexpected that EDTN and PDTN have similar physical/chemical properties. Both are white solids with similar solubility in many types of solvents and have the same thermographic analysis curve. In addition, EDTN and PDTN react almost identically with water, ammonia, alkali, hydrogen and halogens.

The difference in synthesis of EDTN and PDTN is that 1,3 propylenediamine is used for PDTN unlike 1,2 ethylenediamine as described for EDTN above. PDTN is also used as a chemical intermediate. Table 1 compares the physical/chemical properties of EDTN and PDTN.

The similarity in structure, physical/chemical properties and reactivity suggests that the metabolism of EDTN and PDTN will be the same. In both cases, the bond between nitrogen atom and carbon atoms ($N\text{-}CH_2\text{-}CN$) can be broken by hydrolysis whereas the bridge, ($N\text{-}(CH_2)_2\text{-}N$) or ($N\text{-}(CH_2)_3\text{-}N$), is very stable. Therefore, the additional carbon atom in PDTN is not expected to change its metabolism relative to EDTN. The same metabolic pathway of EDTN and PDTN indicates that the toxicity profile of these structurally similar chemicals is expected to be the same. Therefore, the use of PDTN toxicity data for EDTN data gaps should be acceptable.

4.0 EVALUATION OF EXISTING DATA AND PROPOSED TESTING

The available data for PDTN and EDTN have been evaluated below and summarized in Tables 1-3. Since there are no experimental data on EDTN, the experimental data are only from studies on PDTN. Data on EDTN from the EPIWIN computer model were used in the absence of experimental values on PDTN for boiling point, photodegradation and fugacity. EDTN data were also used to compare with PDTN experimental values for other environmental chemistry endpoints to show similarities between the two chemicals and support the use of PDTN data for mammalian toxicity and ecotoxicity endpoints. Robust summaries of the studies are included in this submission. The Klimisch reliability code was used in the robust summaries. A literature search of online data bases including TOXLINE, HSDB and RTECS was searched. There were no studies identified for EDTN or PDTN.

Physical/Chemical Properties:
The melting point for PDTN is 73-74°C. The boiling point using the EPIWIN model for EDTN is 427°C. The density of PDTN is 1.23 g/cm^3. The vapor pressure of PDTN is 1.43×10^{-3} mmHg at 20°C. The log octanol:water partition coefficient (log Kow) of PDTN is –1.3. The water solubility of PDTN is 1.67 g/L. The EPIWIN model for EDTN shows a melting point of 159°C, vapor pressure of 7.54×10^{-8} mmHg at 25°C, a log Kow of –2.17 and water solubility of 1000 g/L. These values for EDTN are consistent with the experimental values of PDTN.

Recommendation: No additional testing is proposed.

Environmental Fate:
AOPWIN was used to estimate the chemical half-life based on an overall OH reaction rate constant. Photodegradation modeling results for EDTN indicate the half-life is estimated to be 4.6 hours.

The hydrolysis half-life of PDTN at pH 4, 7, and 9 at 25°C is estimated to be 5.3, 3.9 and 0.3 years, respectively, based on data at higher temperatures. The EPIWIN model indicates that a hydroysis half-life cannot be estimated for EDTN at 25°C which is consistent with the experimental data on PDTN.

The EPIWIN Level III fugacity model was used to estimate the distribution of EDTN. The modeling results indicate that EDTN primarily distributes to water and soil.

PDTN was biodegraded 0% at day 28 of a Modified Sturm Test. It is considered not readily biodegradable.

Recommendation: No additional testing is proposed.

Aquatic Toxicity:

The 96 hour LC50 in fish and 48 hour EC50 in Daphnia magna for PDTN are greater than 100 mg/L. The 72 hour EC50 for growth inhibition in algae for PDTN is 60 mg/L.

Recommendation: No additional testing is proposed.

Acute Toxicity:

The acute oral and dermal LD50 values in rats for PDTN are greater than 2000 mg/kg. PDTN was not irritating to rabbit skin following a 4 hour exposure and was not sensitizing to guinea pigs in a maximization test.

Recommendation: No additional testing is proposed.

Repeated Dose:

The NOAEL for PDTN in a 28 day oral gavage study in rats was 200 mg/kg/day. At 1000 mg/kg/day, increased liver weight and microscopic changes in the liver were reported.

Recommendation: No additional testing is proposed.

Reproductive/Developmental Toxicity:

There are no reproductive/developmental toxicity data on EDTN or PDTN. A reproductive toxicity study is not required since EDTN is a closed system intermediate.

Recommendation: A teratology study (OECD 414) is proposed for EDTN.

Mutagenicity:

PDTN was not mutagenic in the Ames test or clastogenic in cultured peripheral human lymphocytes in the presence and absence of metabolic activation.

Recommendation: No additional testing is proposed.

TABLE 1: PHYSICAL/CHEMICAL DATA

CAS #	Chemical (Mol. Weight)	MW	MP °C	BP °C	Vapor pressure (mmHg)	Water Sol. (mg/L)	Log Kow	Phys. Appear.
5766-67-6	EDTN (216)	216	159[a]	427[a]	7.54×10^{-8}[a] @25°C	1000000[a] @25°C	-2.17[a]	White crystalline solid
110057-45-9	PDTN (230)	230	73-74	No Data	1.43×10^{-3} @20°C	1670 @18°C	-1.3	White crystalline solid

[a] Data from EPIWIN

TABLE 2: SUMMARY OF ENVIRONMENTAL FATE AND ECOTOXICITY DATA

CAS #	Chemical (Mol. Weight)	Environmental Fate				Ecotoxicity LC50/EC50 (mg/L)		
		Photodeg (hr.).	Stability in water (25°C)	Biodeg.	Trans./ Distr.	Fish	Invert.	Plants
5766-67-6	EDTN (216)	4.6[a]	No Data	No Data	Primarily to soil/water[a]	No Data	No Data	No Data
110057-45-9	PDTN (230)	No Data	5.3 (pH 4), 3.9 (pH 7) and 0.3 (pH 9) years	Not readily biodegrad.	No Data	>100	>100	60 (growth); 129 (rate)

[a] Data from EPIWIN

TABLE 3: SUMMARY OF MAMMALIAN TOXICITY DATA

CAS #	Chemical (Mol. Weight)					Genetic toxicty	
		Acute	Repeated dose	Reproductive	Develop.	Mutagen.	Chrom. Aberr.
5766-67-6	EDTN (216)	No Data	No Data	N/Ap	Test	No Data	No Data
110057-45-9	PDTN (230)	>2 g/kg (oral/ dermal)	NOAEL – 200 mg/kg/day	No Data	No Data	Not mutagenic	Not clastogenic

N/ap – Not applicable for closed system intermediates
Test – OECD 414 study to be done